prognostic indicators—the prognosis for women is significantly better than for men for virtually all anatomic sites and the anatomic site as a prognostic factor varies from least risk (extremities) to greatest risk (head and neck), with the trunk posing an intermediate risk. The designations low-risk primary and high-risk primary are applicable only to the most common forms of cutaneous malignant melanoma—that is, superficial spreading and nodular types—which together constitute about 85% of cutaneous malignant melanomas. Unusual variants or unclassifiable primaries cannot presently be evaluated for risk of recurrence or spread, and microstage measurements with risk factors are used only for research purposes in such cases.

Current "standard" therapy for patients with malignant melanoma presenting in clinical stage I (primary excised, no evidence of metastasis) has been reexcision of the primary site to prevent local recurrence. Such patients have an overall five-year survival of about 80%, a better survival than with most forms of cancer. The prognosis for the low-risk-primary group is a better than 98% five-year survival. Patients with a low-risk primary can be treated with *conservative* reexcision (about a 1-cm radius) of the primary tumor site without risk of local recurrence. Patients with high-risk primaries have a prognosis directly related to their risk factors. Such patients may need a more extensive surgical procedure, including wider reexcision and perhaps elective lymph node dissection. The margins of surgical reexcisions are becoming more conservative, and elective node dissections are done less frequently, as findings from large patient populations continue to question the necessity or benefit of such procedures. Reexcisions requiring a graft for closure should be unnecessary in most cases and should not be undertaken as standard therapy for malignant melanoma per se.

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REFERENCES

Blois MS, Sagebiel RW, Abarbanel RM, et al: Malignant melanoma of the skin—I. The association of tumor depth and type, and patient sex, age, and site with survival. Cancer 1983 Oct 1; 52:1330-1341

Elder DE, Guerry D IV, Heiberger RM, et al: Optimal resection margin for cutaneous malignant melanoma. Plast Reconstr Surg 1983 Jan; 71:66-72

Sagebiel RW: Therapeutic implications of primary malignant melanoma, chap 28, *In* Ackerman AB (Ed): Pathology of Malignant Melanoma. New York, Masson, 1981, pp 353-361

Sexually Transmitted Gastrointestinal Tract Diseases

SEXUALLY TRANSMITTED gastrointestinal tract diseases in homosexual men encompass a number of protozoal, helminthic, viral, bacterial and chlamydial infections. Though several agents may be present simultaneously in one patient, not all of the infections may be symptomatic, but rather represent a carrier state. Most infections cause a nonspecific inflammatory reaction. The intestinal mucosa shows neutrophils in the lamina propria, increased numbers of lymphocytes or plasma cells and occasional crypt abscesses. There are some characteristic findings, however, that can be helpful in making a specific diagnosis. For example, *Giardia* and *Cryptosporidium* predominate in small bowel diseases. The latter organism on hematoxylin-eosin stain appears as a small, round, blue organism (3 to 7 microns) on the microvillous surface. These organisms stain blue with Giemsa. Periodic acid-Schiff and methenamine silver stains are not helpful because both react with mucins at the cell surface.

Viral inclusions should be diligently sought in colonic biopsy specimens, but are not always identified in culture-positive patients. Multinucleate cells and perivascular lymphocytic cuffing have been described with herpes simplex virus. Cytomegalovirus inclusions, nuclear and cytoplasmic types, can be seen in vascular endothelium, in cells in the lamina propria and in epithelium. Parasites such as *Entamoeba histolytica, Strongyloides, Trichuris* and even *Cryptosporidium* may be seen. If the biopsy specimen is from the rectum and if a prominent plasma cell infiltrate or multinucleate giant cells are seen, syphilis (plasma cells) or chlamydial infection (giant cells) should be looked for. These, as well as other bacteria—such as *Yersinia, Campylobacter, Neisseria, Salmonella* and *Shigella*—may simply cause nonspecific findings. Finally, hepatitis B can be sexually transmitted, and hepatitis A is probably transmitted by this route.

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REFERENCES

Baker RW, Peppercorn MA: Gastrointestinal ailments of homosexual men. Medicine (Baltimore) 1982 Nov; 61:390-405

Goodell SE, Quinn TC, Mkrtichian E, et al: Herpes simplex virus proctitis in homosexual men—Clinical, sigmoidoscopic, and histopathological features. N Engl J Med 1983 Apr 14; 308:868-871

Lasser KH, Lewin KJ, Ryning FW: Cryptosporidial enteritis in a patient with congenital hypogammaglobulinemia. Hum Pathol 1979 Mar; 10:234-240

Secondary Diseases in Immunosuppressed Patients

NORMAL FUNCTION of the human immune system requires the interaction of multiple independent cell lines derived from a common pluripotent hematopoietic stem cell. The most important of these cell lines are the T and B lymphocytes and the phagocytes (macrophages and neutrophils). The B lymphocytes produce the specific antibodies required for humoral immunity, the T lymphocytes are primarily responsible for cell-mediated immunity and the macrophages process antigen in addition to their function as phagocytes.

Immune deficiencies may be congenital, iatrogenic or acquired. Patients with these disorders all show unusual susceptibility to infections and have an increased incidence of malignancy. The types of infections are, in a general way, predictive of the portion of the immune system involved. In patients with defects in humoral immunity, or neutropenia, recurrent infections with pyogenic bacteria tend to develop. Defects in cell-mediated immunity frequently result in disseminated viral, fungal and protozoan *(Pneumocystis carinii)* infections. Because of the complicated interactions of the immune system, patients with humoral immune defects may also have problems with viral infections and, conversely, overwhelming bacterial infections may develop

in patients with cell-mediated immune deficits. The most common malignant conditions in which immune deficiency states develop are malignant lymphomas, both Hodgkin's and non-Hodgkin's. Acute leukemias also occur, and the incidence of Kaposi's sarcoma in the recently described acquired immune deficiency syndrome (AIDS) is striking. Other malignant conditions occur but are not increased in incidence above the normal population.

Congenital immunodeficiency states are rare disorders that generally present in childhood, whereas the iatrogenic forms are generally a result of aggressive therapy for malignancy or immunosuppression for transplantation. Until recently, clinically significant acquired immunodeficiency was uncommon; the recent outbreak of AIDS has changed that in many parts of the country.

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REFERENCES

Friedman-Kien AE, Laubenstein LJ, Rubinstein P, et al: Disseminated Kaposi's sarcoma in homosexual men. Ann Intern Med 1982 Jun; 96(Pt 1):693-700

Harris C, Small CB, Klein RS, et al: Immunodeficiency in female sexual partners of men with the acquired immunodeficiency syndrome. N Engl J Med 1983 May 19; 308:1181-1184

Lawton AR III, Cooper MD: Immune deficiency diseases, chap 64, *In* Petersdorf RG, Adams RD, Braunwald E, et al (Eds): Harrison's Principles of Internal Medicine, 10th Ed. New York, McGraw-Hill, 1983, pp 354-362

Mildvan D, Mathur U, Enlow RW, et al: Opportunistic infections and immune deficiency in homosexual men. Ann Intern Med 1982 Jun; 96(Pt 1):700-704

Ziegler JL, Drew WL, Miner RC, et al: Outbreak of Burkitt's-like lymphoma in homosexual men. Lancet 1982 Sep 18; 2:631-633

Cytomegalovirus Infections in Infants

CYTOMEGALIC INCLUSION DISEASE is an infection due to cytomegalovirus, a herpesvirus originally called salivary gland virus. This virus can produce a localized infection, affecting most commonly the gastrointestinal and respiratory tracts, or a generalized infection in which almost any organ may be involved. Histologically, a fairly typical eosinophilic intranuclear inclusion with a clear halo ("owl's eye") can be identified in affected tissues. Occasionally basophilic cytoplasmic granulations are also found.

Infants may acquire the disease in utero, during birth by contamination from the genital canal or by becoming exposed to the virus shortly after birth from sources such as breast milk, tears or other secretions. The infants who appear to be at greater risk are those born to mothers who have acquired a primary infection during gestation.

It is estimated that 0.5% to 2% of the neonates are excreting the virus and that, of these, major complications including central nervous system damage will eventually develop in a significant percentage (10% to 20%). Cytomegalovirus is the most common cause of viral-induced psychomotor retardation. Isolating infants known to be excreting the virus from schools or playgrounds is not practical since many nonidentified children are also excreting the virus.

The most specific and sensitive method for diagnosing a case of cytomegalovirus infection is isolating the virus from tissues, urine, saliva or other body fluids. Detection of IgG antibodies in an infant's blood specimen should be interpreted only in parallel with the mother's IgG antibodies because there is transplacental transfer of this type of antibodies from the mother to the fetus. IgM antibodies do not cross the placenta, but technical problems limit the diagnostic usefulness of routinely measuring their levels.

Vaccines, interferon and several drugs such as acyclovir have been evaluated for the prevention and treatment of cytomegalovirus infections. Although some encouraging results have been obtained, we do not yet have an effective method for controlling this disease.

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REFERENCES

Balfour HH: Prevention and treatment of cytomegalovirus disease, *In* de la Maza LM, Peterson EM (Eds): Medical Virology III. New York, Elsevier Biomedical, 1984, pp 279-312

Stagno S, Pass RF, Dworsky ME, et al: Maternal cytomegalovirus infection and perinatal transmission. Clin Obstet Gynecol 1982 Sep; 25: 563-576

The Role of Coronary Collateral Arteries in Myocardial Ischemia

THE QUESTIONS whether well-developed coronary collateral arteries afford protection to an ischemic myocardium and whether various interventions such as exercise and pharmacologic agents promote collateral development have been studied in numerous experiments. The equivocal findings reflected the great variation in the number of naturally occurring collateral vessels in animals. Recent studies have been conducted in an animal model that has sparse, innate collaterals and a response to exercise stress similar to that seen in humans.

The effects of exercise on collateral development in myocardial ischemia were studied in pigs subjected to critical coronary artery stenosis and then given exercise training. After five months the exercise-trained animals had a greater increase in coronary collateral flow and smaller infarct sizes than their matched sedentary controls. These findings showed that development of the coronary collateral circulation and myocardial tissue salvage are enhanced by exercise training. Thus, exercise during an evolving infarct is effective as an augmentation to collateral growth but is not without risk. If embarked on, it should be conducted only under rigid medical supervision.

The effects of daily aspirin administration on collateral vessel development in cases of myocardial ischemia were studied in pigs subjected to gradual occlusion of a major coronary artery by an Ameroid constrictor. Coronary collateral blood flows were measured at rest and during exercise stress at three days and two months after coronary artery occlusion. The aspirin-treated animals had greater collateral blood flow during exercise stress (61% versus 45% of control; $P<.001$), smaller myocardial infarcts at autopsy (18% versus 32% of the myocardium at risk; $P<.001$) and more prominent collateral development on gross and histologic examinations.

The results of these studies indicate that in an animal